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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/765,026	01/13/1997	MARTINE BARKATS	ST94051-US	5544

7590 09/30/2004

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.
1300 I Street, N.W.
Washington, DC 20005-3315

EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/765,026	BARKATS ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47,61-68,78,79 and 83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47,61-68,78,79 and 83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed July 26, 2004. Amendments were made to the claims. Specifically, claims 69-75, 81 and 82 were cancelled.

Claims 47, 61-68, 78, 79 and 83 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, mailed February 25, 2004, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Claim Rejections - 35 USC § 112

Claims 47, 61-68, 78, 79 and 83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This rejection is maintained for the reasons set forth in the previous Office Action.**

Response to Arguments Concerning Claim Rejections - 35 USC § 112

Applicant's arguments filed July 26, 2004 have been fully considered but they are not persuasive. The following grounds of traversal were presented:

1. Post-filing evidence of enablement, in the form of three scientific publications, was presented (see for example pages 6-7 of Applicant's response). It is concluded that this post-filing

evidence rebuts the evidence provided by the Office in support of the enablement rejection (see for example page 8 of Applicant's response).

2. As it concerns Barkats-2002, it is argued that the survival of dopaminergic neurons can be increased upon expression of SOD-1 from an adenoviral vector (see for example pages 6-7, the bridging paragraph of Applicant's response).

3. As it concerns Barkats-1998, it is argued that a rat model of Parkinson's disease showed expression of hSOD-1 from an adenoviral vector persisted 5 weeks after grafting. It was further argued that there was a minimal immune response associated with the rat model (see for example page 7, first full paragraph of Applicant's response).

4. As it concerns Barkats-1996, it is argued that infection of striatal cells with an adenovirus expressing SOD protect the cells from cell death (see for example page 7, second full paragraph of Applicant's response).

5. It is suggested that the references provided by the Office merely refer to safety considerations inherent to clinical trial issues, and do not reflect the standard of enablement (see for example page 9 of Applicant's response). It is then concluded that the Office "has provided no basis for concluding that the relied upon generalized problems with gene therapy would prevent the skilled artisan from practicing the specific claimed method. The experimental data in the specification, and subsequently supported by Barkats-2002, Barkats-1998, and Barkats-1996, clearly indicate successful Ad delivery and expression of an SOD gene useful to the treatment of Parkinson's disease."

Applicant's arguments are not convincing for the following reasons:

1. It is improper to rely on post-filing evidence to support a conclusion of enablement if the post-filing art does not rely upon the *claimed* method. A US patent is not a hunting license, but rather a reward for the successful completion of an invention. As evidenced by the reliance on post-filing art, further experimentation was required to enable the claimed invention. This further experimentation was conducted for 2, 4 and 8 years, post-filing of the specification, indicating that an undue amount of experimentation was required to enable the claimed invention. As such, the instantly filed specification cannot be considered enabling. The allegation that the evidence set forth in the post-filing art rebuts the position of the Office will be addressed below in a reference-by-reference manner.

2 and 4. As it concerns the expression of SOD in dopaminergic neurons and striatal cells, and their respective survival, it is noted that cell culture results are not predictive of *in vivo* results using an adenoviral vector for gene therapy. Obviously, a cell culture cannot display an immune response, which is a major problem with adenoviral vector-based gene therapy technique. As a result, the findings of Barkats-2002 and Barkats-1996 do not address the predictability of treating Parkinson's disease *in vivo,* using an adenoviral vector. Thus, even if the Barkats-2002 and Barkats-1996 were permissible for establishing the enablement of the instant application post-filing, the recited reference does not address the unpredictability of treating Parkinson's disease.

3. First, it is again pointed out that the teachings of Barkats-1998 are not set forth in the instant specification; it is the enablement of the instant specification that is in question, not the enablement of subsequent publications. Applicant cannot rely on post-filing art to supplement the teachings of the instant specification. Second, it is noted that the Barkats-1998 reference,

while indicating a greater survival of cells expressing SOD following transplantation into rats, clearly indicates that the difference "was not statistically significant" (see specifically, Barkats-1998 sentence bridging the left and right columns of page 336).

Finally, it is noted that the method of administration in Barkats-1998 is via an *ex vivo* grafting method, whereby cells are transfected with the adenovirus *in vitro* and then transplanted into a rat four days after the initial infection. Under such circumstances, one would expect to see only a minimal immunogenic response because the complete organism is not subjected to the initial bolus of adenovirus, to which it would necessarily have an immune response. The fact remains that direct administration of adenovirus (to which the instant specification and claims are directed) results in an immunogenic response, as evidenced by the teachings of Anderson, Verma and Mountain.

5. The references (Verma, Anderson and Mountain) provided by the Office do not simply address safety concerns associated with gene therapy techniques, as alleged. The previous Office action specifically pointed to sections of the Verma, Anderson and Mountain references that discussed areas of unpredictability in performing gene therapy, including maintaining *in vivo* expression of the gene at a therapeutic level, successfully delivering the gene to the cells of interest, and preventing immunogenicity to the delivery vector (which results in decreased expression of the therapeutic gene). None of these issues regard safety concerns, but rather exhibit the unpredictability with practicing the invention, which requires the successful targeting of appropriate cells and sustained expression of the therapeutic gene without induction of an immune response. Thus, Applicant's conclusion that the Office provides no platform for the unpredictability of the claimed invention is simply a blanket statement made without basis.

In conclusion, Applicant is relying on post-filing teachings to enable the claimed invention. This is improper, as a patent must be enabled at the time of filing. Furthermore, the post-filing references upon which Applicant relies do not address the areas of unpredictability established in the art, as taught by the Verma, Anderson and Mountain references supplied by the Office in the previous Office Action. As such, the rejection is maintained for the reasons set forth previously.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
AU 1636

JAMES KETTER
PRIMARY EXAMINER